

## REMARKS

By this Amendment, claim 9 is canceled and claim 10 has been added. No new matter has been added. Claims 8 and 10 are pending.

The present application is directed

- to an apparatus comprising an extruder for making through extrusion particles in the form of spheroids, the said apparatus comprising located at the exit of the extrusion die, a tool, for chopping the filaments obtained by extrusion, the features of the said chopping tool permitting to obtain chopped particles in spheroidal form without any additional spheroidal shaping step,
- to a method of making particles through extrusion, the said method, due to the fact that according to the invention, it comprises, before the extrusion step, a maturing step according to which the mixture to be extruded is maintained during at least 50 minutes in an oven, advantageously in a ventilated tray type oven or in a mixer in order to mature, whereby the mixture to be extruded can be stored for up to 7 days before extrusion, the active principle release curve of the particles obtained through extrusion from said mixture being stabilized and presenting a kinetics slower than that obtained with particles of same composition extruded immediately after making up the mixture without maturing step whereby again the particles obtained by the method including the maturing step introduce into the organism an increased quantity of active substance and at an equivalent rate without increasing the volume of a tablet incorporating said particles.

### **Rejection Under 35 U.S.C. § 102**

Applicants respectfully acknowledge the fact that the rejection of claim 9 under 35 U.S.C. 102(b) as being anticipated by Oshlack et al (WO 96/14058) is withdrawn.

### **Rejection Under 35 U.S.C. § 103**

Claims 8 and 9 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Oshlack et al (WO 96/14058). Claim 9 has been canceled by this Amendment, therefore, Applicant will only address the rejection to claim 8.

With respect to claim 8, the Examiner, while admitting that

*“... WO’ 058 does not teach that the particles are spheroidal...”*

considers that WO’ 058

*“...want to eliminate the spheronization step...”*

and that

*“... by allowing the exit port of the extruder to be any shape so that the multiparticulates can be any shape, this allows the exit port to be a shape that would form spheroidal particulates”.*

It is respectfully submitted that the Examiner’s conclusion drawn from WO’ 058 proceed from a misinterpretation of the said reference.

First of all, WO’ 058 does not teach that they want to eliminate the spheronization step.

On the contrary, WO’ 058 states

page 5, lines 24-26 that the contemplated invention provides

*“...a sustained-release melt extruded multi-particulate formulation which need not be spheronized...”*

and

- page 18, lines 12-14 that

*“...the extrudate may simply be cut into desired lengths and divided into unit doses of the therapeutically active agent without the need of a spheronization step.”.*

That indisputably means that WO’ 058 does not wish to obtain spheroidal particles which explains that a spheronization step is not needed.

Then, the Examiner's contention that the exit port of the extruder is allowed to be of any shape

*"...so that the multiparticulates can be any shape, this allows the exit port to be a shape that would form spheroidal particles..."*

is based on page 17, lines 28-29 of WO' 058, i.e.

*"The melt extruded multiparticulate system can be, for example, in the form of granules, spheroids or pellets depending upon the extruder exit orifice".*

which means that the shape of the multiparticulates obtained, i.e. granules, spheroids or pellets, is a consequence of the shape of the extruder exit orifice.

However, that statement in WO' 058 is technically meaningless.

The skilled artisan knows that extrusion provides a strand and the thus obtained strand is subsequently divided into particles (please see in that respect for instance p. 17, lines 6-9 and lines 17 to 19 of WO' 058).

As indicated page 17, lines 24-25 of WO' 058, the shape of the exit port need not be round but can be oblong, rectangular, etc.

The consequence of that shape of the exit port is that the shape of the strand will have a section which is round, rectangular or oblong.

And the particles obtained from that strand through cutting will thus consist of cylindrically shaped particles which are rectangular or round in section.

Please see also in this connection page 44, lines 5 and 8, claims 2, 3 and 18 (lines 19-24) of WO' 058.

The Examiner's attention is drawn to US Patent 5,965,161 whose priority is claimed in WO' 058, and which is also of interest ; please see in that respect , column 2, lines 42-44, column 6, lines 52-55, column 8, lines 19-40, column 13, lines 23-24, 47-48, column 14, lines 1-2, and 66-67, column 15, lines 28-29 and 58-60 of said US Patent.

From the foregoing explanation, it appears that WO' 058

- does not need a spheronization step because spheroidal particles are not required,
- includes a technically meaningless statement when mentioning that spheroidal particles can be obtained through adaptation of the exit port of the extruder.

On the contrary, in connection with the instant invention, spheroidal particles are preferred.

And it is well known by the skilled artisan that the obtention of spheroidal particles from extruded particles needs performing a spheronization step.

However, due to the particular features of the blades of the chopping tool comprised by the apparatus according to the invention as defined in claim 8, no additional spheronization step is necessary.

And, WO' 058 failing to disclose a method or a device permitting obtention of spheroidal particles without additional spheronization step (which, as indicated hereabove is not needed because spheroidal particles are not required by WO' 058), the invention as defined in instant claim 8 is novel and unobvious over the reference.

Thus the rejection is not founded.

Concerning now new claim 10, the Examiner considers that

*"...although WO' 058 does not specifically refer to a maturing step, it is the position of the examiner that the heating step prior to extrusion, which is discussed by WO' 058, reads on applicant's claimed maturing step."*

That interpretation is respectfully traversed and the Examiner's attention is respectfully drawn to page 23, lines 11 to 22 of WO' 058 from which it appears that the extrudate and the multiparticulates are obtained as follows :

- preparing the mixture to be extruded (lines 13-14),
- charging a powder feeder with the mixture (line 15),
- setting the temperatures of the extruder heating zones to the required temperature,
- starting the feeder, the conveyor and the pelletizer when the heating zones have reached steady temperatures and after the screw rotation speed is set, (lines 18-20),
- extruding the resulting viscous mass as spaghetti-like strands (line 21).

It clearly appears that, when proceeding according to WO' 058, there is no disclosure of a particular heating step distinct from the heating in the extruder heating zones where extrusion is carried out.

The mixture to be extruded is treated when being introduced in the extrusion mechanism proper wherein it is submitted within the room left between the screws to elevation of temperature and to pressure leading to a viscous molten mass which is transported under the action of the screw in direction of the extrusion exit through which it is forced.

On the contrary, the maturing step of the instant invention consists (see page 8, lines 32-36 of the specification)

*“...in maintaining the mixture at a temperature in the range from 20°C to 70°C, preferably in the range from 35°C to 70°C, for 30 minutes to 150 hours, advantageously in a ventilated tray type oven.”.*

During this maturation step, whose duration is of at least 30 minutes and up to 150 hours, the mixture to be subsequently extruded remains in powder form.

During the maturation step which takes place inside an oven for four hours, one day, two days or three days (see example 1, page 13, lines 23-25, 26-28 or 29-31 of the specification) this oven being of course distinct from the extrusion device, unless the extrusion device would be immobilized during maturation; the mixture intended to be extruded is not subjected during maturation to any pressure contrarily to what happens during the extrusion step proper. Actually, during the said extrusion step (see page 9, lines 10-14 of the specification)

*“...the mixture is subjected to the following temperature and pressure conditions :  
- temperature : from 20°C to 200°C, and  
- pressure : from 10 bars to 160 bars.  
It remains in the kneading area for 2 to 6 minutes.”.*

the kneading area corresponding to the extruder heating zones of the device and method disclosed

in WO' 058.

Thus, the maturing and the extrusion steps in the instant invention are obviously distinct from one another and the alleged heating step which according to Examiner exists in WO' 058 in fact does not exist separately, heating and extrusion taking place at the same time.

The Examiner's attention is drawn to the fact that the mixture, when being extruded, remains in the kneading zone for only 2 to 6 minutes during which it is transformed in the above-said viscous mass which is transported to the extrusion exit port.

From the foregoing explanation, it clearly appears that WO' 058 neither discloses nor renders obvious the maturation step according to the invention which surprisingly and unexpectedly leads to the advantages recited in claim 10.

Thus the rejection is not founded.

Applicants respectfully assert that the rejection of claims 8 and 9 as set forth in the Office Action has been addressed and overcome. Applicants further respectfully assert that Claim 8 and new claim 10 are in condition for allowance and request that an early notice of allowance be issued.

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

For at least the reasons set forth above, it is respectfully submitted that the above-identified application is in condition for allowance. Favorable reconsideration and prompt allowance of the claims are respectfully requested.

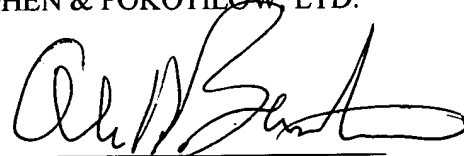
Should the Examiner believe that anything further is desirable in order to place the application in even better condition for allowance, the Examiner is invited to contact Applicants' undersigned attorney at the telephone number listed below.

Respectfully submitted,

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